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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
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(71) Applicant (*for all designated States except US*): UNIVER-
SITA' DEGLI STUDI DI MILANO [IT/TT]; Via Festa del
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(72) Inventors; and

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For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.

(54) Title: METHODS FOR THE SELECTION OF COMPOUNDS USEFUL FOR THE TREATMENT OF HUNTINGTON'S DISEASE

(57) Abstract: The present invention describes a screening method for the identification of molecules useful in the prevention and/or treatment of Huntington's disease characterized by the evaluation of the ability of said molecules of inhibiting the activity of the NRSE sequence; the method is performed by incubating said molecules in a cell system appropriately engineered to detect the level of activation of the NRSE sequence. The invention also describes the process for the preparation of said cell system, the vector used in said process and the use of molecules inhibiting the activity of the NRSE sequence for the preparation of medicaments useful in the treatment and/or prevention of Huntington's disease.

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(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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(57) Abstract: The present invention describes a screening method for the identification of molecules useful in the prevention and/or treatment of Huntington's disease characterized by the evaluation of the ability of said molecules of inhibiting the activity of the NRSE sequence; the method is performed by incubating said molecules in a cell system appropriately engineered to detect the level of activation of the NRSE sequence. The invention also describes the process for the preparation of said cell system, the vector used in said process and the use of molecules inhibiting the activity of the NRSE sequence for the preparation of medicaments useful in the treatment and/or prevention of Huntington's disease.

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 03/01627

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/68 C07K14/47 C12N15/85

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

MEDLINE, EPO-Internal, WPI Data, PAJ, SEQUENCE SEARCH, EMBASE, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	LEE J H ET AL: "Expression patterns of mouse repressor element-1 silencing transcription factor 4 (REST4) and its possible function in neuroblastoma." JOURNAL OF MOLECULAR NEUROSCIENCE: MN. UNITED STATES DEC 2000, vol. 15, no. 3, December 2000 (2000-12), pages 205-214, XP009019742 ISSN: 0895-8696	1,2,5,6,8,11,13
Y	the whole document	3,7
X	WO 96 29433 A (UNIV NEW YORK) 26 September 1996 (1996-09-26)	1,17
Y	page 6 -page 7 page 14 claims 32,37	2,3,5-16

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

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Fax: (+31-70) 340-3016

Authorized officer

Armandola, E

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 03/01627

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MILLECAMPS S ET AL: "Neuron-restrictive silencer elements mediate neuron specificity of adenoviral gene expression." NATURE BIOTECHNOLOGY. UNITED STATES SEP 1999, vol. 17, no. 9, September 1999 (1999-09), pages 865-869, XP001155921 ISSN: 1087-0156	13,14
Y	page 3	15
X	--- TABUCHI AKIKO ET AL: "REST4-mediated modulation of REST/NRSF-silencing function during BDNF gene promoter activation." BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS. UNITED STATES 11 JAN 2002, vol. 290, no. 1, 11 January 2002 (2002-01-11), pages 415-420, XP002259740 ISSN: 0006-291X	13,14
Y	the whole document	15
X	--- TIMMUSK T ET AL: "Identification of brain-derived neurotrophic factor promoter regions mediating tissue-specific, axotomy-, and neuronal activity-induced expression in transgenic mice." THE JOURNAL OF CELL BIOLOGY. UNITED STATES JAN 1995, vol. 128, no. 1-2, January 1995 (1995-01), pages 185-199, XP002259741 ISSN: 0021-9525	13,14
Y	the whole document	1-12, 15-17
Y	--- ZUCCATO C ET AL: "Loss of huntingtin-mediated BDNF gene transcription in Huntington's disease." SCIENCE. UNITED STATES 20 JUL 2001, vol. 293, no. 5529, 20 July 2001 (2001-07-20), pages 493-498, XP002259742 ISSN: 0036-8075	1-17
P,Y	the whole document --- CATTANEO E ET AL: "THE ENIGMA OF HUNTINGTON'S DISEASE" SCIENTIFIC AMERICAN, SCIENTIFIC AMERICAN INC. NEW YORK, US, vol. 287, no. 6, December 2002 (2002-12), pages 60-65, XP001155743 ISSN: 0036-8733 last two paragraphs page 65 --- -/--	1-17

INTERNATIONAL SEARCH REPORT

International Application No
PC 1/IB 03/01627

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>GARCÍA-SÁNCHEZ RUBÉN ET AL: "Identification of repressor element 1 in cytochrome P450 genes and their negative regulation by RE1 silencing transcription factor/neuron-restrictive silencer factor." BIOCHIMICA ET BIOPHYSICA ACTA. NETHERLANDS 17 MAR 2003, vol. 1620, no. 1-3, 17 March 2003 (2003-03-17), pages 39-46, XP009019760 ISSN: 0006-3002 figure 5</p>	13,14
T	<p>FUSCO FRANCESCA R ET AL: "Co-localization of brain-derived neurotrophic factor (BDNF) and wild-type huntingtin in normal and quinolinic acid-lesioned rat brain." THE EUROPEAN JOURNAL OF NEUROSCIENCE. FRANCE SEP 2003, vol. 18, no. 5, September 2003 (2003-09), pages 1093-1102, XP001154711 ISSN: 0953-816X the whole document</p>	
T	<p>ZUCCATO CHIARA ET AL: "Huntingtin interacts with REST/NRSF to modulate the transcription of NRSE-controlled neuronal genes." NATURE GENETICS. UNITED STATES SEP 2003, vol. 35, no. 1, September 2003 (2003-09), pages 76-83, XP001155920 ISSN: 1061-4036</p>	

Continuation of Box I.2

Claims Nos.: 18

Present claim 18 relates to an extremely large number of possible compounds for which support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is not found. The claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

national application No.
PCT/IB 03/01627

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 18
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 03/01627

Patent document cited in search report		Publication date		Patent family member(s)	Publication date
WO 9629433	A	26-09-1996	AU	5369396 A	08-10-1996
			WO	9629433 A1	26-09-1996